

ASCO Poster

Anti-PSMA mAb HuJ591 Specifically Targets Tumor Vascular Endothelial Cells in Patients with Advanced Solid Tumor Malignancies.

Monoclonal antibody huJ591 recognizes the extracellular domain of prostate specific membrane antigen (PSMA_{ext}). In addition to prostate epithelial cells, immunohistochemical studies show that PSMA is also expressed by vascular endothelial cells of numerous solid tumors, but not by normal vascular endothelium in benign tissues or in neoplastic epithelial cells of non-prostate malignancies. We initiated an IRB approved Phase I dose escalation trial of ¹¹¹Indium-labeled huJ591 to test the hypothesis that PSMA is a target for huJ591 vasculotoxic therapy; to define huJ591 toxicity and MTD in non-prostate cancer patients; to determine pharmacokinetics and biodistribution of huJ591; and to assess for HAHA. Eligible patients include those with refractory solid tumor malignancies whose tumor types are known to express PSMA on the neovasculature. Nine patients received 5mg (3 patients) or 10mg (6 patients) of ¹¹¹In-huJ591 followed by a second dose 14 days later. Toxicity consisted of infusion reactions including one patient with grade 3 bronchospasm. Pre-medication with acetaminophen and diphenhydramine prevented further reactions. Indium scanning showed localization of huJ591 to tumor sites in 6/9 patients. No objective responses occurred, however, a colon cancer patient had a 50% decline in CEA and two patients had improvement in cancer pain and performance status. Based on these data, the protocol was revised to provide dosing for 6 consecutive weeks (10, 20, 40 and 80 mg/week dose levels) with the option for re-treatment on 8 week cycles if patients have stable or responding disease. Six patients are receiving treatment on this schedule. HuJ591 specifically targets vascular endothelial cells of solid tumors including renal, bladder and colon cancer. MAb huJ591 may be an effective approach to target vascular endothelial cells of solid tumors with radioactivity or other cytotoxins. Support: CaPCURE, BZL Biologics.

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